

Remarks

Claims 1-10, 14-64, and 66-70 were pending in the subject application. By this Amendment, claims 1-70 have been canceled, and new claims 71-140 have been added. The undersigned avers that no new matter is introduced by this amendment. Entry and consideration of the amendments presented herein is respectfully requested. Accordingly, claims 71-140 are currently before the Examiner for consideration. Favorable consideration of the pending claims is respectfully requested.

The applicants and the applicants' representative wish to thank Examiner Woitoch for the courtesy of the telephonic interview conducted with the undersigned on February 12, 2004, regarding the rejections under 35 U.S.C. §112, first and second paragraphs. The remarks and amendments set forth herein are consistent with the substance of the interview and are believed to address the outstanding issues as discussed during the interview.

The applicants gratefully acknowledge the Examiner's indication at page 2 of the Office Action that the requirement for an election of species is withdrawn.

By this Amendment, the applicants have canceled claims 1-70 and added claims 71-140. Support for this Amendment can be found throughout the specification and claims as originally filed. Support for claims 75, 76, 103, 104, 109, and 110 can be found, for example, at page 12, paragraph 48, and page 13, paragraph 49, of the specification. Support for claims 85, 86, and 126 can be found, for example, at page 3, paragraph 8, page 6, paragraph 18, page 9, paragraph 34, and page 12, paragraph 45, of the specification.

The specification has been objected to for lacking the required sequence identifiers. The applicants have reviewed the specification for sequences lacking an identifier. By this Amendment, the applicants have amended page 4, paragraph 11, to insert SEQ ID NOs. 25-28. The Brief Description of the Sequences section at page 10 of the specification has been updated accordingly. In addition, submitted herewith is a Submission and substitute Sequence List on paper and in computer readable format. The substitute Sequence List contains SEQ ID NOs 25-28. The applicants submit that no new matter is introduced by this amendment. Therefore, reconsideration and withdrawal of the objection is respectfully requested.

Claims 1-10, 14-64, and 66-70 have been objected to because their scope has not been amended in accordance with the elected subject matter and also due to certain informalities. As indicated above, by this Amendment, the applicants have canceled claims 1-10, 14-64, and 66-70, and added new claims 71-140. It should be understood that this amendment has been made in accordance with the elected subject matter and the applicants expressly reserve the right to pursue the invention(s) disclosed in the subject application, including any subject matter canceled or not pursued during prosecution of the subject application, in a related application. The applicants respectfully submit that claims 71-140 are consistent with the elected subject matter (Group II). Therefore, reconsideration and withdrawal of the objection is respectfully requested.

Claims 1-3, 5-9, 13-54, 58-61, and 63-67 have been objected to for not being the object of a sentence. By this Amendment, the applicants have amended the Claims section of the specification to recite "We claim". Therefore, reconsideration and withdrawal of the objection is respectfully requested.

Claims 1-10, 14-64, and 66-70 are rejected under 35 U.S.C. §112, first paragraph, as lacking sufficient written description. The applicants respectfully submit that the claimed invention is fully described by the subject specification. However, by this Amendment, claims 1-10, 14-64, and 66-70 have been canceled, rendering these rejections moot.

As discussed during the Examiner interview, claims 71-140 recite that the polynucleotide encodes a pesticidal polypeptide comprising the amino acid sequence of SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:6, SEQ ID NO:8, SEQ ID NO:10, SEQ ID NO:12, SEQ ID NO:14, SEQ ID NO:16, SEQ ID NO:18, SEQ ID NO:20, SEQ ID NO:22, SEQ ID NO:23, or SEQ ID NO:24. The new claims do not recite the terms "NPF polypeptide" or "functional equivalents". Polynucleotides encoding the recited pesticidal polypeptide would be readily envisioned by those of ordinary skill in the art. Thus, the applicants respectfully submit that the specification would convey to one of ordinary skill in the art that the applicant was in possession of the claimed subject matter at the time the application was filed. Accordingly, in view of the foregoing remarks, the applicant respectfully requests reconsideration and withdrawal of the rejection under 35 U.S.C. §112, first paragraph.

Claims 1-10, 14-64, and 66-70 are rejected under 35 U.S.C. §112, first paragraph, as non-enabled. The applicants respectfully submit that the claimed invention is fully enabled by the subject specification.

The Office Action indicates that the specification does not provide adequate guidance as to how to make the subject invention because there is no clearly defined minimal structure for NPF polypeptides. As indicated above, new claims 71-140 recite that the polynucleotide encodes a pesticidal polypeptide comprising the amino acid sequence of SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:6, SEQ ID NO:8, SEQ ID NO:10, SEQ ID NO:12, SEQ ID NO:14, SEQ ID NO:16, SEQ ID NO:18, SEQ ID NO:20, SEQ ID NO:22, SEQ ID NO:23, or SEQ ID NO:24. At page 8, the Office Action indicates that “there is no evidence of record that Applicants possess any pesticidal effective compositions according to the elected invention”. At pages 9 and 10, the Office Action indicates that the only working example demonstrating a biological effect for an NPF polypeptide of the subject invention was an assay in which mosquitoes were injected with NPF I and NPF II. However, as discussed during the Examiner interview, this is not correct. Examples 1 and 2 at pages 25-27 of the subject specification describe the effects of pesticidal polypeptides of the subject invention on trypsin biosynthesis, and mortality in mosquito larvae. Table 2 at pages 26-27 of the specification provides experimental results obtained *in vivo*, demonstrating the pesticidal activity of the polypeptides recited in the claims. The experimental data in Table 2 was also submitted with an Expert Declaration under 37 C.F.R. §1.132 by Dr. Dov Borovsky (one of the co-inventors of the subject invention) in the parent application, serial no. 09/295,849, on January 16, 2001 and February 7, 2001. The contents of Dr. Borovsky’s Declaration concerning the experimental data is incorporated herein by reference.

The Office Action makes reference to the difficulties in predicting whether a given peptide can exhibit functional activity in a non-native species. As indicated in Example 2 of the specification, NPF polypeptides of the subject invention have been identified in the Colorado potato beetle, cockroach, fruit fly, and mosquito. Synthetic polypeptides corresponding to the wild-type polypeptides of three of these four insects, as well as other variants of these polypeptides, were ingested by first instar *A. aegypti* larvae. Lethality was demonstrated by polypeptides from all three insects investigated. Hence, NPF polypeptides identified within the orders Coleoptera (beetle),

Dictyoptera (cockroach), and Diptera (fly) exhibited pesticidal activity toward *A. aegypti* larvae, a dipteran. This supports the teaching of the specification that the pesticidal polypeptides can be used to control pests that are heterologous to the insects from which the polypeptides were derived. Furthermore, as taught in Examples 4 and 5 of the specification, pesticidal activity of the polypeptides toward a particular pest can be readily confirmed using standard bioassay procedures. The applicants respectfully submit that such screening procedures do not constitute undue experimentation.

The Office Action notes that endogenous amidation activity has not been observed in some of the recited pest food cells, such as prokaryotes or lower eukaryotes, and asserts that the subject specification does not teach how to design an expression vector that can express an amidated polypeptide. Claims 71-140 recite that the polynucleotide encodes a pesticidal polypeptide comprising the amino acid sequence of SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:6, SEQ ID NO:8, SEQ ID NO:10, SEQ ID NO:12, SEQ ID NO:14, SEQ ID NO:16, SEQ ID NO:18, SEQ ID NO:20, SEQ ID NO:22, SEQ ID NO:23, or SEQ ID NO:24, which are non-amidated.

The Office Action also questions whether the polypeptides of the subject invention are stable in the peptidase-rich pest gut and, relying on various references, suggests that C-terminal amidation may be required to impart biological activity to the polypeptides of the invention. However, as shown in Table 2 at pages 26 and 27 of the specification, both amidated and non-amidated polypeptides exhibited similar activity and, in some cases, non-amidated polypeptides exhibited even higher pesticidal activity (*i.e.*, lower LC₅₀ values) than their amidated counterparts. Furthermore, the experimental results shown in Table 2 of the specification demonstrate that synthetic non-amidated polypeptides as small as four amino acids in length proved stable in the pest gut long enough to exhibit pesticidal activity. Given the peptidase-rich environment within the pest gut, it would be expected that the polypeptides of the subject invention would be sufficiently stable to survive expression by a transformed cell.

Notwithstanding the aforementioned experimental data, the Office Action cites Rao *et al.*, which discloses the efficient expression of the 5 amino acid long proctolin peptide in a tobacco plant using an expression construct containing tandemly arranged repeats of oligonucleotides which code for a polypeptide multimer having several copies of neuropeptide units separated by endoproteolytic

cleavage sites. At page 16, the Office Action points out that proctolin was chosen by Rao *et al.* because its biologically active form is not C-terminally amidated or blocked at its N-terminus and the Office Action further asserts that “there are no such analogous features ascribed to NPF I and NPF II.” However, as shown in Table 2 of the specification, non-amidated polypeptides of the subject invention are pesticidally active, and new claims 71-140 recite non-amidated amino acid sequences. Therefore, the applicants respectfully submit that one of ordinary skill in the art would be able to recombinantly express polynucleotides encoding the pesticidal polypeptides of the subject invention, given the level of ordinary skill in the art at the time the invention was made. In view of the foregoing remarks, the applicants respectfully request reconsideration and withdrawal of the rejection under 35 U.S.C. §112, first paragraph.

Claims 1-10, 14-64, and 66-70 have been rejected under 35 U.S.C. §112, second paragraph, as being indefinite. The applicants respectfully submit that the claims are not indefinite. However, by this Amendment, claims 1-10, 14-64, and 66-70 have been canceled, rendering this rejection moot.

The Office Action indicates that claim 1 is incomplete in not relating back to the preamble, and that it is unclear how the pest is controlled. Control of a pest is achieved by application of a pesticidally effective amount of the agent of the subject invention. As discussed during the Examiner interview, new claim 71 recites a pesticidally effective amount of transformed cells expressing a polynucleotide encoding the pesticidal polypeptide are applied to the pest, or to a pest-inhabited locus. Additionally, claim 71 recites that the pest ingests the pesticidal polypeptide. Thus, the relationship between the method steps and the objective is clearly established. The terms “pesticidal” and “pesticidally effective” are defined at page 9, paragraphs 30 and 31, of the subject specification. As the Examiner is undoubtedly aware,

It is here where the definiteness of the language employed must be analyzed—not in a vacuum, but always in light of the teachings of the prior art and of the particular application disclosure as it would be interpreted by one possessing the ordinary level of skill in the pertinent art. *In re Angstadt*, 190 USPQ 214, 217 (C.C.P.A. 1976)

Therefore, the applicants respectfully submit that one of ordinary skill in the art, when reading the claims in light of the specification, would be able to ascertain with a reasonable degree of precision and particularity the area set out and circumscribed by the claims.

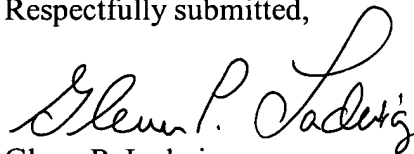
New claims 71-140 do not recite the terms "NPF polypeptide", "functional equivalent", or "optimized for expression". Accordingly, reconsideration and withdrawal of the rejection under 35 U.S.C. §112, second paragraph, is respectfully requested.

In view of the foregoing remarks and amendments to the claims, the applicants believe that the currently pending claims are in condition for allowance, and such action is respectfully requested.

The Commissioner is hereby authorized to charge any fees under 37 C.F.R. §§ 1.16 or 1.17 as required by this paper to Deposit Account 19-0065.

The applicants invite the Examiner to call the undersigned if clarification is needed on any of this response, or if the Examiner believes a telephonic interview would expedite the prosecution of the subject application to completion.

Respectfully submitted,



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Attachments: Submission of Sequence Listing under 37 C.F.R. §§1.821-1.825
Sequence Listing on paper and computer readable format (disk)